REMARKS

Claims 1-15 and 36-63 are in this application. Claims 1-15 and 36-41 have been withdrawn from consideration. Claims 16-35 have been canceled and replaced by new claims 42-63. Support for the new claims is shown in the table below:

Claim	Support
42	original claim 16; page 16, lines 14-17
43	original claim 16; page 16, lines 14-17
44	page 7, line 6
45	page 7, lines 17-18, page 13, page 2, line 26, claim 24
46	original claim 17
47	original claim 18, page 4, lines 17-20
48	original claim 19
49	original claim 20
50	original claim 22
51	original claim 23
52	original claim 24
53	original claim 25
54	original claim 26
55	original claim 27
56	original claim 28
57	original claim 29
58	original claim 30
59	original claim 31
60	original claim 32
61	original claim 33
62	original claim 34
63	original claim 35

Page 1 of the specification has been amended to correct an incorrect citation. The abstract of JP 56166124 A2 was submitted in an Information Disclosure Statement and has been considered by the Examiner.

Page 5 has been amended to correct a typographical error.

Page 8 has been amended to insert the ATCC accession number HTB-22 before the cell line MCF7.

The amendments on page 8, last paragraph and on page 16 are supported by the disclosure on page 2, lines 24-26.

The Examiner has rejected claims 16-35 under 35 USC 112, first paragraph. Applicants respectfully traverse this rejection.

The Examiner states that because of the use of the term microorganisms in the claims, the claims are not enabling. Applicants respectfully disagree. However, to expedite prosecution, the word microorganisms in the claims has been replaced by bacteria. Claims have also been added to limit the bacteria to feces-derived bacteria. This is supported on page 7, lines 5 to 18. A claim defining the bacteria as *E. coli, S. bovis* and *Enterococcus* has also be added.

As discussed below, the word "early" has been deleted from the claims. On page 2, lines 24-27 it is explained that "healthy individuals were shown to present a higher percentage of *Escherichia coli* with cancerolytic activity as compared to the microflora of cancer patients. "On page 3, lines 12-16 it is stated "The term 'early diagnosis of cancer' as used herein interchangeably with the terms 'early detection of cancer', 'cancer screening' or 'confirmation of cancer' is intended to convey such diagnosis, whether or not the cancer has reached the stage in which it is detectable by other methods presently available to the clinician." In addition on page 3, lines 8-11 it is explained that the relative fractions of the microorganisms in the sample are indicative of the presence or absence of cancer in the subject.

Therefore, it is respectfully requested that this rejection be withdrawn.

The Examiner has rejected Claim 33 under 35 USC 112, first paragraph. Applicants respectfully traverse this rejection.

The Examiner states that the specification lacks complete deposit information for the deposit of cells having the Accession No. ATCC MCF7. MCF7 is available from ATCC under their accession number HTB-22. A copy of the pages from the ATCC on-line catalog for this cell line is attached. Claim 61 includes the ATCC accession number HTB-22.

Therefore, it is respectfully requested that this rejection be withdrawn.

The Examiner has rejected claims 16-35 under 35 USC 112, second paragraph as being indefinite. Applicants respectfully traverse this rejection.

The term *"early diagnosis"* of cancer is understood to those in the art as *"diagnosis of the cancer at a sufficiently early stage to allow its curing, or at least alleviating by local modality, such as surgery or radiation"*. Although the possibility to diagnose cancer in its early stage is an advantage of the invention this method is not limited thereto, therefore, and the word *"early"* has been deleted from the claims.

Claim 42 includes a diagnosis step (diagnosing said subject as having or not having cancer in accordance with the TCNI value determined in (vii).) Support for this amendment is found *inter alia* on page 16, lines 14-17.

Therefore, it is respectfully requested that this rejection be withdrawn.

The Examiner has rejected claim 12 on the basis that there is insufficient basis for the limitation "a corresponding sample" in the claim. Applicants respectfully traverse this rejection.

Firstly, claim 12 has been withdrawn from consideration by the Examiner.

Secondly, claim 12 does not include the phrase "a corresponding sample."

Thirdly, the phrase "corresponding sample" is used in claim 4 and is defined on page 6, lines 13-15.

Therefore, it is respectfully requested that this rejection be withdrawn.

The Examiner has rejected claim 18 because of the use of the phrase "undesirable contamination." Applicants respectfully traverse this rejection.

This phrase is described on page 4, lines 17-25 of the specification.

Therefore, it is respectfully requested that this rejection be withdrawn.

The Examiner has rejected claim 32 because of the use of the phrase "standard culture of cancer cells." Applicants respectfully traverse this rejection.

The phrase "standard culture of cancer cells" is a well understood by a person skilled in the art to be "a continuously growing cell culture established from a human cancer."

Therefore, it is respectfully requested that this rejection be withdrawn.

The Examiner has rejected claims 16-32 and 34-35 as being

anticipated by Karapetian (US Patent 5,344,762). Applicants respectfully traverse this rejection.

Contrary to the Examiner's allegations, Karapetian does not anticipate the invention. There are at least three features that distinguish the present invention over the reference:

The present invention recites, (in steps (iv) of claim 42) ***determining for each of said types of bacteria*** [identified in the feces-derived sample] ***its relative fraction from the total count of bacteria in said sample or in a corresponding sample***. Such a step does not exist in Karapetian, and therefore, the reference fails to anticipate all of the claim's limitations.

Furthermore, the present invention recites, (in steps (vi) of claim 42) *preparing a diagnostic sample containing bacteria of the types isolated, the fraction of each of the bacteria types in said diagnostic sample corresponds to the fraction thereof in the fecal sample, as determined in step (iv).* Such a step is also absent from the teaching of Karapetian, and therefore, the presently claimed invention includes another limitation not taught by the cited reference.

The present invention also recites, (in steps (v) of claim 42) *isolating bacteria of said one or more types from said sample.* Karapetian does not teach such an isolation step. Karapetian does teach (see col. 1 line 59 to col. 2 line 2) "a method...wherein a human **feces-derived sample** of bacteria ... is subjected to incubation in vitro with a standard culture of cancer cells..." (emphasis added).

It is admitted that Example 1 of Karapetian uses the term *isolation* in the context of feces-derived bacteria. However, *isolation* is described in said Example 1 as inoculating portions of the feces sample on plain agar (to "isolate" *E. Coli*) and agar-agar (to "isolate" *Streptococcus faecalis*) media. Such a procedure does not isolate one type of bacteria from others, as these kinds of agar media are not selective.

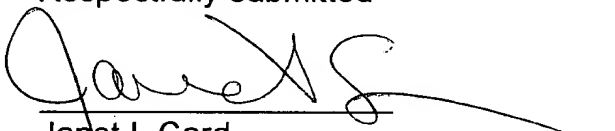
Therefore, the reference is at least non-enabling to an isolation step. Furthermore, the teaching of *the reference as a whole* is to incubate a feces-derived sample of bacteria with a standard culture of cancer cells, as recited in claim 1 of Karapetian, with no isolation step.

New claim 43 takes the claimed invention even further from Karapetian by reciting the use of *more than one* type of bacteria. When more than one type of bacteria are used, it must be acknowledged that the claimed method is novel over Karapetian.

Therefore, it is respectfully requested that the rejection be withdrawn.

Applicants submit that the present application is in condition for allowance and favorable consideration is respectfully requested. If any outstanding issues remain, the examiner is respectfully requested to telephone the undersigned.

Respectfully submitted



Janet I. Cord
c/o Ladas & Parry
26 West 61st Street
New York, New York 10023
Reg. No. 33, 778 (212-708-1935)

MARKED-UP COPY

In the Specification

Please replace paragraph 3 on page 1 with the following:

> Among previous proposals for the diagnosis of cancer may be mentioned the following. In U.S. Pat. No. 3,476,514 there was described a method of detecting cancer cells by staining test cells with acriflavine-HCl solution, determining indirectly the dye absorbed by the test cells and comparing with a control JP [54,143,528] 56166124A2 proposed a method for diagnosing malignant tumors which utilized an injectable composition containing an endotoxin extracted from cultured bacteria. In GB 1587244, there was described *inter alia,* the use in a serum agglutination test on the sera of patients, for the detection of neoplasm, of an antigen produced by a species of the genus Streptococcus.

Please replace 3rd full paragraph 2 on page 5 with the following:

> Figures **2A-2B** are pictures obtained by microscope of cancer cells treated with the diagnostic sample of the present invention, the diagnostic samples derived either from a healthy object (Fig. 2A) or [form] from a cancer patient (Fig. 2B).

Please replace paragraph 2 on page 8 with the following:

> The cancer cells employed may be any standard culture of cancer cells, for example ATCC HTB-22 (MCF7) . The interaction of the bacteria mixture with the cancer cells includes incubation of the bacteria and cancer cells under conditions suitable for the bacteria to act on the cells. These conditions include suitable temperature (e.g. 37°C), and a time period (in the following examples, 4 hours), sufficient to determine the extent of interaction between the bacteria and the cancer cells, the extent of interaction is determined by the degree of lysis of the cancer cells by the bacteria mixture (the diagnostic sample). This may be observed, for example, by the aid of

a microscope or an Automated Computer Assisted Microscope, wherein the number of remaining cancer cells is counted.

Please replace paragraph 3 on page 8 with the following:

Figures 2A and 2B show microscope pictures obtained after incubation of cancer cells with a bacterial sample obtained from a healthy subject, (Fig, 2A) or from a cancer patient (Fig.2B.) These pictures show that in the presence of a bacterial sample obtained from sick [healthy] subject, only a few cancer cells remain, i.e. there is an effective lysis of the cancer cells by the bacteria.

Please replace paragraph 3 on page 16 with the following:

Fig. 2A and 2B show microscope pictures of the result of incubation of bacteria samples obtained from cancer patients or healthy subjects (diagnostic samples as prepared by the method of the present invention) with the standard cancer cells. In particular, a larger amount of viable cancer cells are visualized in the culture treated with a sample obtained from [sick] healthy subject (Fig. 2[A]B), as compared to the result obtained with a bacteria sample obtained from [sick] healthy subject (Fig. 2A[B]).